November 7, 2002

Chris Ford
Q.A. Manager
Cardolite Corporation
500 Doremus Avenue
Newark, N.J. 07105

Dear Mr. Ford:

The Office of Pollution Prevention and Toxics is transmitting EPA's comments on the robust summaries and test plan for Cashew Nut Shell Liquid, posted on the ChemRTK HPV Challenge Program Web site on June 28, 2002. I commend the Cardolite Corporation for its commitment to the HPV Challenge Program.

EPA reviews test plans and robust summaries to determine whether the reported data and test plans will provide the data necessary to adequately characterize each SIDS endpoint. On its HPV Challenge Web site, EPA has provided guidance for determining the adequacy of data and preparing test plans used to prioritize chemicals for further work.

Please note that EPA encourages Challenge Program sponsors who have proposed acute oral toxicity testing to use an *in vitro* dose range-finding protocol to set the starting dose for the Up and Down test (OECD TG 425). Information on this protocol is available at http://www.epa.gov/chemrtk/toxprtcl.htm.

EPA will post this letter and the attached comments on the HPV Challenge Web site within the next few days. As noted in the comments, we ask that the Cardolite Corporation advise the Agency, within 60 days of this posting on the Web site, of any modifications to its submission.

If you have any questions about this response, please contact Richard Hefter, Chief of the HPV Chemicals Branch, at 202-564-7649. Submit questions about the HPV Challenge Program through the "Contact Us" link on the HPV Challenge Program Web site pages or through the TSCA Assistance Information Service (TSCA Hotline) at (202) 554-1404. The TSCA Hotline can also be reached by e-mail at tsca-hotline@epa.gov.

I thank you for your submission and look forward to your continued participation in the HPV Challenge Program.

Sincerely,

/s/

Oscar Hernandez, Director
Risk Assessment Division

Attachment

cc: C. Auer
A. Abramson
M. E. Weber

EPA Comments on Chemical RTK HPV Challenge Submission: Cashew Nut Shell Liquid

SUMMARY OF EPA COMMENTS

The sponsor, Cardolite Corporation, submitted a test plan and robust summaries for Cashew Nut Shell Liquid (CNSL, CAS No. 8007-24-7) to EPA on June 5, 2002. EPA posted the submission on the Chemical RTK HPV Challenge Web site on June 28, 2002.

EPA has reviewed the submission and has reached the following conclusions:

1. Physicochemical Properties and Environmental Fate. EPA agrees with the submitter's approach for melting point, boiling point, water solubility, partition coefficient and stability in water. EPA disagrees with the submitter that data are not necessary for vapor pressure, biodegradation, photodegradation, and fugacity. The submitter needs to test CNSL for vapor pressure and ready biodegradation and provide estimated photodegradation and fugacity data for cardanol and cardol, the primary components of CNSL.

2. Health Effects. EPA agrees with the submitter's approach to these endpoints. The submitter needs to address deficiencies in the robust summaries for the genetic toxicity studies.

3. Ecological Effects. EPA disagrees that the predicted values for the two main chemical components of CNSL (cardanol and cardol) will adequately characterize the endpoints. EPA believes that the chemical will exhibit chronic toxicity in aquatic organisms and that aquatic chronic testing is necessary.

EPA requests that the submitter advise the Agency within 60 days of any modifications to its submission.

EPA COMMENTS ON THE CASHEW NUT SHELL LIQUID CHALLENGE SUBMISSION

Test Plan

Chemistry (melting point, boiling point, vapor pressure, partition coefficient, and water solubility).

The submitter's approach to melting point, boiling point, partition coefficient and water solubility is adequate for the purposes of the HPV Challenge Program.

Vapor Pressure. The submitter states in the test plan that estimation of the vapor pressures of the two main components of CNSL and their analogs using EPIWIN predicts the vapor pressure to be less than 2×10^{-5} Pa (or 1.5×10^{-7} mm Hg) at ambient temperatures, which it claims is negligible, and that experimental measurement is inappropriate. The submitter did not supply details of its calculations. EPA calculated a vapor pressure range of 1.47×10^{-7} Pa (1.1×10^{-9} mm Hg) to 1.7×10^{-4} Pa (1.3×10^{-6} mm Hg) for CNSL (EPIWIN) using its two main components (cardanol and cardol). According to OECD Guideline 104, accepted methods are available for measuring vapor pressure down to 10^{-5} Pa. In view of the uncertainty in the estimated value, EPA believes that the submitter needs to provide measured data for this endpoint in robust summary format. (OECD guidance states in one place that measurement is necessary down to 10^{-5} kPa. The correct reference point is 10^{-5} Pa (10^{-8} kPa)).

Environmental Fate (photodegradation, stability in water, biodegradation, fugacity).

Photodegradation. No data were provided for this endpoint. The submitter states that "due to the extremely low vapor pressure under ambient conditions, there is essentially no opportunity for CNSL to enter the atmosphere, thus photodegradation is irrelevant." The submitter further states that "as photodegradation is estimated as part of the model used to calculate the transport and distribution..., difficulties in providing the correct inputs to the model mean that it is not possible to derive a meaningful value for this endpoint." The latter statement is incorrect. Calculation of photodegradation using AOPWIN is based only on the molecular structure and does not require physicochemical data. The EPA-estimated vapor pressure of 1.1×10^{-9} to 1.3×10^{-6} mm Hg at 25 °C suggests that CNSL is a semivolatile organic (compounds with a vapor pressure of ~ 7.6 x 10(-2 to -9) mm Hg) and can exist partially as vapor or adsorbed to particles. The submitter needs to provide estimated data for this endpoint in robust summary format for cardanol and cardol.

Stability in water. The submitter's approach to stability in water is adequate for the purposes of the HPV Challenge Program.

Biodegradation. Distilled CNSL was reported to be "readily biodegradable" under aerobic conditions. The study was reported to follow OECD Guideline 302D and GLP. However, this draft guideline determines inherent biodegradability in the Concawe test, and includes a preacclimation step. The draft guideline states that this test has enhanced degradation power over a ready test and "is usually performed only after failure to pass a test for ready." Therefore, the submitter needs to test CNSL for ready biodegradability following OECD TG 301.

Fugacity. No data were provided for this endpoint. The submitter indicates that the required inputs to the model are either not available or not feasible to determine. EPA disagrees. Fugacity should be estimated for the primary components of CNSL, cardanol and cardol. These chemicals are expected to have similar transport and partitioning behavior in the environment based on their structures and physicochemical properties. The submitter needs to provide estimated data for this endpoint for cardanol and cardol in robust summary format.

Health Effects (acute toxicity, repeated-dose toxicity, genetic toxicity, and reproductive/ developmental toxicity).

EPA agrees with the submitter's proposal to conduct testing for acute, repeated-dose, reproductive, and developmental toxicity endpoints. The submitter needs to address deficiencies in the robust summaries for the genetic toxicity studies.

Ecological Effects (fish, invertebrate and algal toxicity).

EPA believes that these high log Kow chemicals (> 8.0) will not exhibit acute aquatic toxicity. The ECOSAR program predicted no effects at the chemical's water solubility. Although a 21-day daphnia study is the usual chronic test, fish is the aquatic species most sensitive to phenols. For this reason, EPA recommends a 90-day rainbow trout study to satisfy the concern for chronic toxicity. More information on testing difficult chemicals such as poorly water-soluble substances can be found in the Guidance Document on Aquatic Toxicity Testing of Difficult Substances and Mixtures (OECD, June 2000) available on the OECD website at http://www.oecd.org/ehs/test/monos.htm.

Specific Comments on the Robust Summaries

Health Effects.

Information missing for the genetic toxicity (*in vitro*) studies includes the composition and purity of the test material, Cardolite NC 511. Although the composition of generic distilled CNSL is given in the test plan, it is not clear how closely Cardolite NC 511 corresponds to this composition.

Follow-up Activity

EPA requests that the submitter advise the Agency within 60 days of any modifications to its submission.